Remarks

Claims 1-7 are pending in the subject application and currently before the Examiner. By this Amendment, Applicants have amended claims 1 and 3 and added new claim 8. Support for the amendments can be found throughout the subject specification, including, for example, at page 3, lines 13-15 and lines 26-27. Entry and consideration of the amendments and new claim presented herein is respectfully requested. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants note that a Claim of Priority Under 35 USC §119 was included with the filing materials when the subject application was mailed to the Patent Office on August 10, 2001. In accordance with MPEP 201.14(b), Applicants reaffirmed their claim to foreign priority and requested that the foreign priority application submitted in the parent application, U.S. application Serial No. 08/792,415, be made of record in the subject application. However, the Office Action Summary page of the instant Action did not include an acknowledgement of Applicants' claim to foreign priority under 35 USC §119 or that the foreign priority documents were received. Accordingly, Applicants respectfully request that their claim to foreign priority be acknowledged and the foreign priority documents be made of record by the Examiner in the subject application.

Claims 1 and 5 are rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that the recitation in the claims that "racemization proceeds in favor of the *threo* diasteriomer" lacks antecedent basis and an enabling description. In view of this, the Examiner requires removal of the "new matter." Applicants respectfully assert that there is adequate written description in the subject specification and the recitation that "racemization proceeds in favor of the *threo* diasteriomer" does not constitute new matter. However, by this Amendment, Applicants have amended claim 1 to delete reference to the language objected to by the Examiner. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §112, first paragraph, is respectfully requested.

Claims 1-3 and 6 are rejected under 35 USC §103(a) as obvious over Shaflee (1969) in view of Barry (1993) or Miller (1980) and Miller (U.S. Patent No. 4,254,261). In addition, claims 1-6 are

rejected under 35 USC §103(a) as obvious over Shaflee (1969) in view of Barry (1993) or Miller (1980) and Miller (U.S. Patent No. 4,254,261) further in view of Rometsch (U.S. Patent No. 2,957,880). Further, claims 1-7 are rejected under 35 USC §103(a) as obvious over Shaflee (1969) in view of Barry (1993) or Miller (1980) and Miller (U.S. Patent No. 4,254,261) further in view of Rometsch (U.S. Patent No. 2,957,880) and further in view of Jacques (1981) supplemented with Harris (U.S. Patent No. 6,242,464). Applicants respectfully traverse these grounds of rejection.

Applicants respectfully maintain that the claimed invention is not obvious over the cited references, regardless of whether the references are taken alone or in combination. Applicants acknowledge that the Miller and Barry references disclose racemization of a cyclic amino acid (specifically, 6-oxo-2-piperidine-carboxylic acid) and an amino acid ester, respectively. However, as Applicants have indicated in their Amendment dated December 19, 2000 submitted in the parent application (Serial No. 08/792,415), the substrate in the Barry reference has only one chiral center. Similarly, there is only one chiral center in substrate disclosed in the Miller references. These references do not teach or suggest racemization of compounds having two stereogenic centers, such as methylphenidate. As discussed at page 2, lines 8-9, of the subject specification, the subject invention is based on the surprising discovery of means to effect racemization of both chiral centers of methylphenidate. It is only the subject application that teaches means for effectively racemizing a single enantiomer of methylphenidate such that all four stereoisomers are produced.

As during prosecution of the parent application, the Examiner apparently assumes that racemization of any methylphenidate enantiomer will occur at both chiral centers of the molecule so as to produce all four possible stereoisomers. With all due respect to the Examiner, Applicants respectfully assert this assumption is incorrect, as is apparent from the Rometsch patent. Although Example 6 of the Rometsch patent discloses epimerisation with base, only one chiral center of the molecule is racemized with the result that less than all of the four possible stereoisomers are produced. Thus, Applicants respectfully assert that the prior art does not teach or suggest a means for racemization of a single enantiomer of methylphenidate wherein all four stereoisomers of methylphenidate are obtained. Moreover, the prior art teaches away from Applicant's claimed invention in that the Rometsch patent teaches that racemization of methylphenidate occurs at only one of the two chiral centers of the molecule. If the substrate is racemized at only one chiral center,

the product of racemization does not contain the enantiomer that is the specified product of claim 1. This makes the known racemization procedure unsuitable for the recycling process encompassed by claim 1. Applicants respectfully assert that, at the time of the present invention, it was not predictable that they would be able to identify conditions under which all four stereoisomers could be produced from a single enantiomer of methylphenidate.

In addition, Applicants note that the chiral centers of methylphenidate are located on adjacent atoms and are not of a similar type. Consideration of this molecular structure would suggest to the ordinarily skilled artisan that one chiral center can be racemized much more easily than the other, thereby leading to production of fewer than the four possible stereoisomers. This is borne out by the experimental evidence in Rometsch. The effectiveness of Applicants' claimed invention in racemizing methylphenidate is, therefore, surprising. Accoordingly, Applicants respectfully assert that the cited references do not teach or suggest the claimed invention, nor do they provide the requisite reasonable expectation of success in obtaining the invention. Reconsideration and withdrawal of the rejections under 35 USC §103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

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Docket No. GJE-136D1
Serial No. 09/928,139

Marked-Up Version of Amended Claims

Claim 1 (amended):

1. A process for obtaining single enantiomer *d-threo*-methylphenidate or *l-threo*-methylphenidate, which comprises resolution of a mixture of the *d-threo*-methylphenidate and *l-threo*-methylphenidate enantiomers; racemisation of the unwanted enantiomer, to give a mixture of all four stereoisomers, wherein the racemisation comprises reacting the unwanted enantiomer with an acid; enriching said mixture following racemisation wherein [the equilibrium of said racemisation proceeds in favor of] the *d-threo* and *l-threo* stereoisomers of methylphenidate are enriched over the *d-erythro* and *l-erythro* stereoisomers of methylphenidate; and separation of [the] said *d-erythro* and *l-erythro* stereoisomers, to leave the said mixture of *d-threo*-methylphenidate and *l-threo*-methylphenidate enantiomers for resolution.

Claim 3 (amended):

3. The process, according to claim 1, wherein the racemisation comprises heating the unwanted enantiomer with an achiral carboxylic acid [a carboxylic acid, wherein said carboxylic acid is achiral].

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Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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Attachment: Marked-Up Version of Amended Claims

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